SEQUENCE LISTING

<110> Sharma et al.

<120> SOLUBLE NOTCH-BASED SUBSTRATES FOR GAMMA SECRETASE AND METHODS AND COMPOSITIONS FOR USING SAME

<130> 28341/01130

<160> 17

<170> PatentIn version 3.1

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<212> DNA

<213> Artificial sequence

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Met Asp Ile Ala Val Glu Ala Gly Asn Leu Ala Gln Ala Ile Gly Arg 305 310 315 320

Asn Gly Gln Asn Val Arg Leu Ala Ser Gln Leu Ser Gly Trp Glu Leu 325 330 335

Asn Val Met Thr Val Asp Asp Leu Gln Ala Lys His Gln Ala Glu Ala 340 345 350

His Ala Ala Ile Asp Thr Phe Thr Lys Tyr Leu Asp Ile Asp Glu Asp 355 360 365

Phe Ala Thr Val Leu Val Glu Glu Gly Phe Ser Thr Leu Glu Glu Leu 370 375 380

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Asp Lys Ser Pro Gly Ala Arg Gly Ser Glu Phe Asn Ile Pro Tyr Lys 545 550 560

Leu His Leu Met Tyr Val Ala Ala Ala Ala Phe Val Leu Phe Phe 580 585 590 Val Gly Cys Gly Val Leu Leu Ser Arg Lys Arg Arg Arg Gln His Gly Gln Leu Trp Phe Pro Glu Gly Phe Lys Val Ser Glu Ala Ser Lys Lys 610 615 620 Lys Arg Arg Glu Pro Leu Gly Glu Asp Ser Val Gly Leu Lys Pro Leu Lys Asn Ala Ser Asp Gly Ala Leu Met Asp Asp Asn Gln Asn Glu Trp Gly Asp Glu Asp Leu Glu Thr Lys Lys Phe Arg Phe Glu Glu Pro Val 660 665 670 Val Leu Pro Asp Leu Ser Asp Gln Thr Asp His Arg Gln Trp Thr Gln Gln His Leu Asp Ala Ala Asp Leu Arg Met Ser Ala Met Ala Pro Thr Pro Pro Gln Gly Glu Val Asp Ala Asp Asp Tyr Lys Asp Asp Asp Asp 705 710 715 720 Lys His His His His His His His <210> <211> 525 <212> DNA Artificial sequence <213> <220> <223> Wildtype notch DNA sequence <400> 3 aatatteett acaagattga ggeegtgaag agtgageegg tggageetee getgeeeteg 60 120 cagetgeace teatgtacgt ggeageggee geettegtge teetgttett tgtgggetgt 180 ggggtgctgc tgtcccgcaa gcgccggcgg cagcatggcc agctctggtt ccctgagggt 240 ttcaaagtgt cagaggccag caagaagaag cggagagagc ccctcggcga ggactcagtc ggcctcaagc ccctgaagaa tgcctcagat ggtgctctga tggacgacaa tcagaacgag 300 tggggagacg aagacctgga gaccaagaag ttccggtttg aggagccagt agttctccct 360 gacctgagtg atcagactga ccacagacag tggacccagc agcacctgga cgctgctgac 420 ctgcgcatgt ctgccatggc cccaacaccg cctcaggggg aggtggatgc tgacgattat 480 525 aaagacgatg acgataaaca ccatcaccat caccatcacc attga <210> <211> 174 <212> PRT <213> Artificial sequence <220> <223> Wildtype notch protein sequence

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Arg Arg Gln His Gly Gln Leu Trp Phe Pro Glu Gly Phe Lys Val Ser 50 55 60	£
Glu Ala Ser Lys Lys Lys Arg Arg Glu Pro Leu Gly Glu Asp Ser Val 65 70 75 80	L
Gly Leu Lys Pro Leu Lys Asn Ala Ser Asp Gly Ala Leu Met Asp Asp 85 90 95	Ç
Asn Gln Asn Glu Trp Gly Asp Glu Asp Leu Glu Thr Lys Lys Phe Arg 100 105 110	j
Phe Glu Glu Pro Val Val Leu Pro Asp Leu Ser Asp Gln Thr Asp His 115 120 125	3
Arg Gln Trp Thr Gln Gln His Leu Asp Ala Ala Asp Leu Arg Met Ser 130 135 140	<i>:</i>
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- His Val Pro Glu Arg Leu Ala Ala Gly Thr Leu Val Leu Val Val 1565 1570 1575
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- Ser Leu His Asn Gln Thr Asp Arg Thr Gly Glu Thr Ala Leu His 1910 1920
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- Glu Ser Pro His Gly Tyr Leu Ser Asp Val Ala Ser His Pro Leu 2195 2200 2205
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- Leu Pro Gly Met Pro Asp Thr His Leu Gly Ile Ser His Leu Asn 2225 2230 2235
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Thr His Thr Gly Pro Asn Cys Glu Arg Pro Tyr Val Pro Cys Ser Pro 210 215 220

Ser Pro Cys Gln Asn Gly Gly Thr Cys Arg Pro Thr Gly Asp Val Thr 225 230 235 240

His Glu Cys Ala Cys Leu Pro Gly Phe Thr Gly Gln Asn Cys Glu Glu 245 250 255

Val Asp Gly Val Asn Thr Tyr Asn Cys Pro Cys Pro Pro Glu Trp Thr 275 280 285

Gly Gln Tyr Cys Thr Glu Asp Val Asp Glu Cys Gln Leu Met Pro Asn 290 295 300

Ala Cys Gln Asn Gly Gly Thr Cys His Asn Thr His Gly Gly Tyr Asn 305 310 315 320

Cys Val Cys Val Asn Gly Trp Thr Gly Glu Asp Cys Ser Glu Asn Ile 325 330 335 Asp Asp Cys Ala Ser Ala Ala Cys Phe His Gly Ala Thr Cys His Asp 340 345 350 Arg Val Ala Ser Phe Tyr Cys Glu Cys Pro His Gly Arg Thr Gly Leu 355 360 365 Leu Cys His Leu Asn Asp Ala Cys Ile Ser Asn Pro Cys Asn Glu Gly 370 380 Ser Asn Cys Asp Thr Asn Pro Val Asn Gly Lys Ala Ile Cys Thr Cys 385 390 395 400 Pro Ser Gly Tyr Thr Gly Pro Ala Cys Ser Gln Asp Val Asp Glu Cys 405 410 415Ser Leu Gly Ala Asn Pro Cys Glu His Ala Gly Lys Cys Ile Asn Thr 420 425 430 Leu Gly Ser Phe Glu Cys Gln Cys Leu Gln Gly Tyr Thr Gly Pro Arg 435 440 445Cys Glu Ile Asp Val Asn Glu Cys Val Ser Asn Pro Cys Gln Asn Asp 450 460Ala Thr Cys Leu Asp Gln Ile Gly Glu Phe Gln Cys Met Cys Met Pro Gly Tyr Glu Gly Val His Cys Glu Val Asn Thr Asp Glu Cys Ala Ser 485 490 495Ser Pro Cys Leu His Asn Gly Arg Cys Leu Asp Lys Ile Asn Glu Phe Gln Cys Glu Cys Pro Thr Gly Phe Thr Gly His Leu Cys Gln Tyr Asp 515 520 525 Val Asp Glu Cys Ala Ser Thr Pro Cys Lys Asn Gly Ala Lys Cys Leu 530 540 Asp Gly Pro Asn Thr Tyr Thr Cys Val Cys Thr Glu Gly Tyr Thr Gly 545 550 560 Thr His Cys Glu Val Asp Ile Asp Glu Cys Asp Pro Asp Pro Cys His 565 570 575Tyr Gly Ser Cys Lys Asp Gly Val Ala Thr Phe Thr Cys Leu Cys Arg 580 585 590Pro Gly Tyr Thr Gly His His Cys Glu Thr Asn Ile Asn Glu Cys Ser 595 600 605Ser Gln Pro Cys Arg Leu Arg Gly Thr Cys Gln Asp Pro Asp Asn Ala 610 $\,$ 620 Tyr Leu Cys Phe Cys Leu Lys Gly Thr Thr Gly Pro Asn Cys Glu Ile 625 630 635 640As nLeu Asp Asp Cys Ala Ser Ser Pro Cys Asp Ser Gly Thr Cys Leu 645 650 655Asp Lys Ile Asp Gly Tyr Glu Cys Ala Cys Glu Pro Gly Tyr Thr Gly 660 665 670

Ser Met Cys Asn Ser Asn Ile Asp Glu Cys Ala Gly Asn Pro Cys His 675 680 685Asn Gly Gly Thr Cys Glu Asp Gly Ile Asn Gly Phe Thr Cys Arg Cys 690 695 700 Pro Glu Gly Tyr His Asp Pro Thr Cys Leu Ser Glu Val Asn Glu Cys 705 710 715 720 Asn Ser Asn Pro Cys Val His Gly Ala Cys Arg Asp Ser Leu Asn Gly 725 730 735 Tyr Lys Cys Asp Cys Asp Pro Gly Trp Ser Gly Thr Asn Cys Asp Ile 740 745 750Asn Asn Glu Cys Glu Ser Asn Pro Cys Val Asn Gly Gly Thr Cys $755 \hspace{1cm} 760 \hspace{1cm} 765$ Lys Asp Met Thr Ser Gly Ile Val Cys Thr Cys Arg Glu Gly Phe Ser 770 780 Gly Pro Asn Cys Gln Thr Asn Ile Asn Glu Cys Ala Ser Asn Pro Cys 785 790 795 800 Leu Asn Lys Gly Thr Cys Ile Asp Asp Val Ala Gly Tyr Lys Cys Asn 805 810 815 Cys Leu Leu Pro Tyr Thr Gly Ala Thr Cys Glu Val Val Leu Ala Pro 820 825 830 Cys Ala Pro Ser Pro Cys Arg Asn Gly Gly Glu Cys Arg Gln Ser Glu 835 840 845 Asp Tyr Glu Ser Phe Ser Cys Val Cys Pro Thr Ala Gly Ala Lys Gly 850 855 860 Gln Thr Cys Glu Val Asp Ile Asn Glu Cys Val Leu Ser Pro Cys Arg 865 870 875 880 His Gly Ala Ser Cys Gln Asn Thr His Gly Xaa Tyr Arg Cys His Cys 885 890 895 Gln Ala Gly Tyr Ser Gly Arg Asn Cys Glu Thr Asp Ile Asp Asp Cys 900 905 910 Arg Pro Asn Pro Cys His Asn Gly Gly Ser Cys Thr Asp Gly Ile Asn 915 920 925 Thr Ala Phe Cys Asp Cys Leu Pro Gly Phe Arg Gly Thr Phe Cys Glu 930 935 940 Glu Asp Ile Asn Glu Cys Ala Ser Asp Pro Cys Arg Asn Gly Ala Asn 945 950 955 960 Cys Thr Asp Cys Val Asp Ser Tyr Thr Cys Thr Cys Pro Ala Gly Phe 965 970 975 Ser Gly Ile His Cys Glu Asn Asn Thr Pro Asp Cys Thr Glu Ser Ser 980 985 990

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- Leu Cys Pro Pro Gly Phe Thr Gly Ser Tyr Cys Gln His Val Val 1010 1015 Tyr Cys Gln His Val Val
- Asn Glu Cys Asp Ser Arg Pro Cys Leu Leu Gly Gly Thr Cys Gln 1025 1030 1035
- Asp Gly Arg Gly Leu His Arg Cys Thr Cys Pro Gln Gly Tyr Thr 1040 1045 1050
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- Cys Lys Asn Gly Gly Lys Cys Trp Gln Thr His Thr Gln Tyr Arg 1070 1075 1080
- Cys Glu Cys Pro Ser Gly Trp Thr Gly Leu Tyr Cys Asp Val Pro 1085 1090 1095
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- Ala Arg Leu Cys Gln His Gly Gly Leu Cys Val Asp Ala Gly Asn 1115 1120 1125
- Thr His His Cys Arg Cys Gln Ala Gly Tyr Thr Gly Ser Tyr Cys 1130 1135 1140
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- Cys Glu Cys Arg Ala Gly His Thr Gly Arg Arg Cys Glu Ser Val

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Leu Arg Glu Leu Ser Arg Val Leu His Thr Asn Val Val Phe Lys

1600

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1910 1915 1920

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Tyr Ser 1940		Ser	Asp	Ala	Ala 1945		Arg	Leu		Glu 1950		Ser	Ala
Asp Ala 1955		Ile	Gln	Asp	Asn 1960	Met	Gly	Arg	Thr	Pro 1965	Leu	His	Ala
Ala Val 1970		Ala	Asp		Gln 1975	Gly	Val	Phe	Gln	Ile 1980		Ile	Arg
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Pro Leu 2000		Leu	Ala	Ala	Arg 2005	Leu	Ala	Val	Glu	Gly 2010	Met	Leu	Glu
Asp Leu 2019		Asn	Ser	His	Ala 2020		Val	Asn	Ala	Val 2025	Asp	Asp	Leu
Gly Lys 2030		Ala	Leu	His	Trp 2035		Ala	Ala		Asn 2040		Val	Asp
Ala Ala 204		Val	Leu	Leu	Lys 2050		Gly	Ala	Asn	Lys 2055		Met	Gln
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Ser Tyr 207		.Thr	Ala		Val 2080		Leu	Asp		Phe 2085		Asn	Arg
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Glu Arg 210		His	His	Asp	Ile 2110	Val	Arg	Leu	Leu	Asp 2115	Glu	Tyr	Asn
Leu Val 2120		Ser	Pro	Gln	Leu 2125	His	Gly	Ala	Pro	Leu 2130	Gly	Gly	Thr
Pro Thr 213		Ser	Pro	Pro	Leu 2140		Ser	Pro	Asn	Gly 2145	Tyr	Leu	Gly
Ser Leu 2150		Pro	Gly	Val	Gln 2155	Gly	Lys	Lys	Val	Arg 2160		Pro	Ser
Ser Lys 216		Leu	Ala	Суѕ	Gly 2170	Ser	Lys	Glu	Ala	Lys 2175	Asp	Leu	Lys
Ala Arg 2180		Lys	Lys	Ser	Gln 2185	Asp	Gly	Lys	Gly	Cys 2190		Leu	Asp
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Ile Asp Arg Lys Ser Gly Asp Phe Asp Thr Phe Arg Arg Trp Leu Val

Val Asp Glu Val Thr Gln Pro Thr Lys Glu Ile Thr Leu Glu Ala Ala 65 70 75 80

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Val 145	Asn	Arg	Asp	Asn	Ile 150	Ser	Leu	Asp	Leu	Gly 155	Asn	Asn	Ala	Glu	Ala 160
Val	Ile	Leu	Arg	Glu 165	Asp	Met	Leu	Pro	Arg 170	Glu	Asn	Phe	Arg	Pro 175	Gly
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Ala	Gln	Leu 195	Phe	Val	Thr	Arg	Ser 200	Lys	Pro	Glu	Met	Leu 205	Ile	Glu	Leu
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Ala	Arg	Val	Gln 260	Ala	Val	Ser	Thr	Glu 265	Leu	Gly	Gly	Glu	Arg 270	Ile	Asp
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Ile	Ala	Gln	Ala 420	Gln	Glu	Glu	Ser	Leu 425	Gly	Asp	Asn	Lys	Pro 430	Ala	Asp
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435 440 445

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Ser Gly Ser Gly His His His His His Ser Ala Gly Lys Glu Thr $500 \hspace{1.5cm} 505 \hspace{1.5cm} 510$

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Gly Leu Val Pro Arg Gly Ser Ala Gly Ser Gly Thr Ile Asp Asp Asp 530 535 540

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